Original Article

COPD AWARENESS SURVEY: DO BELGIAN PULMONARY PHYSICIANS COMPLY WITH THE GOLD GUIDELINES 2010?

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ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is underestimated, underdiagnosed and often undertreated in the general population. A survey of 17 structured questions, delivered to all Belgian pulmonary physicians (PPs) (116 responses), evaluated diagnosis and treatment strategies in accordance with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines 2010 and assessed opinions about the importance of diurnal variation of COPD symptoms. All COPD diagnoses (37% new cases) were spirometry confirmed. Main diagnostic parameters were symptoms (99%), external risk factors (99%), clinical examination (97%), exacerbations (96%) and patient mobility (96%). FEV_1 (forced expiratory volume in 1s) (97%) or FEV_1/FVC (ratio of FEV_1 to forced vital capacity) (93%) were used most to assess diagnosis and severity. The 3 most important therapeutic objectives were symptom relief, preventing exacerbations, and improving quality of life; if these were not reached, the preferred strategy (60% of PPs) was adding another medication. Treatment strategies varied with COPD stage: short-acting β_2-agonists (90%) and short-acting anti-cholinergics (59%) were used for GOLD I disease, whereas for higher stages long-acting β_2-agonists (36-48%) and long-acting anti-cholinergics (79%) were given with inhaled corticosteroids (21-67%). Symptoms were perceived to vary throughout the day, affecting quality of life (97%) and mobility (89%). In particular, respiratory symptoms were more severe in the morning (51-92%), leading PPs to adapt treatment (69%). This survey demonstrated that management of COPD by PPs in Belgium is generally in line with the GOLD guidelines 2010 and that they perceive morning symptoms as being frequent and having an impact on patient's life.

Key words: COPD, pulmonary physicians, symptoms, treatment strategy, survey

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality worldwide. It is accompanied by a negative impact on quality of life resulting in serious economic and social burden (1). Yet, its prevalence remains underestimated as most patients with stage I (mild COPD) do not present with any symptoms or with symptoms that are perceived as normal (2-4). A systematic review performed in 1996 reported a pooled COPD prevalence of 7.6% for the 28 countries included in the analysis (1, 5). The international Burden of Obstructive Lung Disease (BOLD) study showed that, when

stages II and higher of COPD are confirmed by spirometry, the overall prevalence of these stages is 10%, which is greater than typically reported (6). The Global Initiative for Chronic Obstructive Lung Disease (GOLD) was set up to increase awareness of COPD and the GOLD report (published in 2001, updated in 2006, 2010 and 2011) provided recommendations for the management of COPD[3]. Many different reasons are given by physicians for non-adherence to the GOLD guidelines 2010. For instance, lack of familiarity with the guidelines, low self-efficacy, and time constraints have been reported as important barriers to adherence (7).

In a COPD survey conducted in Austria where diagnosis was confirmed by spirometry, Schirnhofer et al. (8) found that GOLD stage I and higher affected 26% of the participants and GOLD stage II and higher 11%. By contrast, the prevalence of doctor-diagnosed chronic bronchitis, emphysema, or COPD in the same population was only 6%. In view of such a high discrepancy between general practice screening for COPD and diagnosis based on objective lung function measures such as spirometry, Schirnhofer et al. (8) concluded that awareness of COPD among health professionals was suboptimal and needed to be improved.

Observational studies, conducted in Spain (9) and in the USA (10), identified significant variation in the percentage of diagnostic spirometries performed in primary care centers, with more than a threefold difference between the lowest and highest rates of use.

In Belgium, Vandevoorde et al. (11) revealed "an important prevalence of undiagnosed COPD" among current smokers: 17.1% of the patients included had an established COPD diagnosis, while the spirometry screening determined a prevalence of 46.6% in the same population. Office spirometry significantly improves early detection of COPD (12), as screening for airflow obstruction almost doubles the number of known patients with obstructive lung disease.

The cornerstones of treatment strategies commonly used by specialists include pharmacotherapy and rehabilitation in addition to smoking cessation. There is accumulating evidence that pharmacotherapy should be started early in the course of the disease (13-15). This measure is important as decline in both physiological and quality of life aspects occur at a considerably faster rate in the early stages of the disease (15-16). Combination pharmacotherapies including anticholinergics, corticosteroids and β_2-agonists are the leading treatment strategies (17-18), while non-pharmacological strategies take an important part in the management of advanced COPD (19).

Diurnal variations in peak expiratory flow have been reported for COPD patients (20-21), which are weakly negatively correlated to dyspnoea and fatigue (22). COPD symptoms also vary throughout the day, affecting daily activities especially in the morning (23). In a telephone survey, later expanded through the internet, Partridge et al. (24-25) revealed that the majority of COPD patients experienced breathlessness, phlegm, cough, wheezing and chest tightness in the morning, while admitting they were not taking their medication in time for it to exert its optimal effect.

However, as this is a recent finding, most physicians may not be aware of the impact of morning symptoms on patients' lives.

In the present study, we surveyed Belgian pulmonary physicians (PPs) in order to assess their self-declared diagnosis and treatment strategies for COPD, in accordance with the GOLD guidelines 2010, and their opinion about the importance of morning symptoms for the initiation of treatment and its follow-up.

METHODS

This survey took place in 2010 and was open to all PPs practicing in Belgium (N = 468). Participation to the survey was voluntary and no incentive was offered for answering the questionnaire. Data were collected using a structured questionnaire with closed questions available in French or Dutch (available in the Online Supplemental material; an English translation is provided in the Appendix). The questionnaire was designed by a group of Belgian experts called the COPD Working Group. It was attached to the invitation for a series of AstraZeneca COPD Awareness Meetings ("The quest for GOLD – COPD in different dimensions") and delivered by AstraZeneca sales representatives during their regular visits to the PPs during the first two quarters of 2010. All questionnaires were provided with a prepaid envelope to be sent back to M. Decramer, prinicipal investigator of the study before the 15th of June, 2010.

A cover letter from the COPD Working Group accompanied the questionnaire and outlined the objectives of the survey: to understand the diagnosis and treatment strategies used in COPD patients in usual clinical practice and to explore opinions about symptom variation throughout the day in COPD patients. In addition, the cover letter specified that all information provided would be treated anonymously and combined with the information of other PPs to provide an overall analysis for Belgium.

Extra questionnaires were available at the meetings in case the participating physicians had not had the opportunity to respond previously: they were able to complete the survey before the presentation and the questionnaires were directly sent to the prinicipal investigator.

The PPs were asked to answer the questionnaire based on either their usual clinical practice, or, for some specific questions, the treatment of their last 10 new COPD patients. Two general questions requested the number of years of professional experience and the geographic location for the PP. The main questionnaire was divided into two parts, each based on one of the objectives outlined in the cover letter. The first part was related to the patients and was divided into five main sections:

- Origin of the patient
- Diagnosis and assessment of severity
- Therapeutic goals
- Treatment strategy
- Patient follow-up.

Each of these sections contained questions that requested further information regarding the usual clinical practice of the PPs. The use of the GOLD guidelines 2010 by the PPs was asked in the sections on diagnosis and assessment of severity and treatment strategy. The second part of the questionnaire was related to the variability of symptoms and was divided into five questions:

- Do you think that COPD symptoms vary throughout the day?
- If yes, at what time of day are they at their most serious?

– Do you think the variability of symptoms throughout the day impacts the quality of life of COPD patients?
– Do you think that morning symptoms impact the mobility of the patient?
– If you indicated that symptoms are most severe in the morning, does this impact your therapeutic approach?

Responses to the questionnaire were collected and analysed by G. Gayan-Ramirez at the KULeuven. Missing answers were not replaced. The data was summarised as mean ± standard deviation or the percentage of respondents answering the question.

RESULTS

Out of the 468 PPs that were contacted, 116 questionnaires were returned and analyzed (response rate = 25%, Table 1). The average practice experience was 15.7 ± 9.9 years and the respondents treated on average 72 ± 52 COPD patients per month. The responses came from all geographical areas of Belgium, except Walloon Brabant, with a higher proportion from the provinces Antwerp (23%), Liège (16%), and Hainaut (14%); the other provinces were evenly represented except for Luxembourg (2%).

Patient referral

Most patients had been previously diagnosed with COPD (63%) and were referred by their general practitioner (GP) (51%) or by another PP (16%). One third of patients came on their own initiative (33%).

Table 1: Demographic characteristics of respondents

		N
Contacted	100%	468
Answered	25%	116
Practice experience	15.7 ± 9.9 years	113
Patients per month	72 ± 52	113
Geographical area		116
Antwerp	23%	
Liège	16%	
Hainaut	14%	
Brussels	10%	
Flemish Brabant	8%	
East-Flanders	7%	
West-Flanders	6%	
Limburg	5%	
Namur	5%	
Unknown	4%	
Luxemburg	2%	
Walloon Brabant	0%	

Parameters used to diagnose COPD

All PPs confirmed the COPD diagnosis with spirometry and the vast majority made the diagnostic themselves (84%) or got it from another specialist [not a PP] (4%), while a minority (12%) relied on the diagnostic of a GP. Most patients were diagnosed with a GOLD II (41%) or a GOLD III (31%) stage; the remaining patients were divided equally between GOLD I and GOLD IV stages (14% each).

FEV_1 (forced expiratory volume in one second) alone or ratio of FEV_1 to FVC (forced vital capacity) were used by nearly all PPs to assess both diagnosis and severity (Table 2), while the percentage of FEV_1 reversibility was used less often and mainly for diagnosis. Nearly all PPs used a combination of lung function, symptoms, external risk factors, clinical examination, occurrence of exacerbation and patient's mobility as diagnostic criteria (Table 3); other commonly used criteria included co-morbidities and quality of life.

Family history and external risk factors were mainly used for diagnosis, while the patient's mobility, the MRC (Medical Research Council) dyspnoea scale, co-morbidities, quality of life and frequency of exacerbations were more commonly used to assess the severity of COPD.

Among the symptoms used as diagnostic criteria, dyspnoea, frequent or persistent cough, and sputum production/expectorations were most often cited (Table 3). Smoking was more frequently (41%) stated as a specific risk factor than exposure to chemical substances (23%) or air pollution (22%) and asthma (14%).

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Therapeutic objectives

We asked the PPs to choose the three most important therapeutic objectives from a list of 12 items: symptoms relief, improvement of morning symptoms, prevention of respiratory function decline, prevention of exacerbations, prevention of hospitalisation, prevention of oral corticosteroids use, prevention of antibiotics use, mortality reduction, prevention or reduction of treatment side effects, prevention and treatment of COPD complications, improvement of quality of life, improvement of patients' mobility (ability to carry out daily tasks), or other. Those selected the most were symptoms relief,

Table 2: Spirometry parameters used to diagnose COPD

Spirometry parameters	Used by PPs (%)	For diagnosis only (%)	For severity only (%)	For both (%)
FEV_1 (% of predicted value)	97	2	16	82
FVC (% of predicted value)	58	22[a]	8[a]	70[a]
FEV_1 / FVC	93	33[a]	3[a]	64[a]
% of FEV_1 reversibility	74	44[a]	11[a]	45[a]

Data analyzed according to the information recorded in the returned questionnaires (N = 116).
COPD: Chronic Obstructive Pulmonary Disease
FVC: forced vital capacity; FEV_1: forced expiratory volume in one second.
[a] N = 115

Table 3: Parameters used in the diagnosis of COPD

Diagnosis parameters	Used by PPs (%)	For diagnosis only (%)	For severity only (%)	For both (%)
Pulmonary function	100	1	3	96
Exposure to external risk factors	99	54	7	39
Smoking	41			
Chemical substances	23			
Pollution	22			
Asthma	14			
Symptoms	99	14[a]	8[a]	78[a]
Dyspnoea	19			
Frequent/persistent cough	16			
Sputum expectorations	16			
Wheezing	12			
Tightness	12			
Morning symptoms	11			
Nocturnal awakening	7			
Fatigue	6			
Others	1			
Physical examination	97	15	17	69
Occurrences of exacerbation	96	4	43	53
Patient's mobility	96	3	61	36
Co-morbidities	82	8	54	38
Quality of life	72	5	50	45
Family history of COPD	46	65	10	25
MRC dyspnoea scale	33	16[b]	55[b]	29[b]
Other	20	15	60	25

Data analysed according to the information recorded in the returned questionnaires (N = 116).
MRC: Medical Research Council.
COPD: Chronic Obstructive Pulmonary Disease
[a] N = 114
[b] N = 115

prevention of exacerbations, and improvement of quality of life. If the PPs could not reach their objectives, 60% of them would add another medication, 14% would increase the doses, and 10% would switch medication; but 16% would choose another treatment modification. When asked what other type of treatment modification, they answered: rehabilitation (61%), another inhalation system (11%), integrated care (11%), observation (8%), and improving compliance (8%).

Treatment strategies

The treatment of newly diagnosed COPD patients was usually initiated by a PP (in 62% of cases), or by a GP (34% of cases), rarely by a specialist in another domain (5%).

The PPs modulated their treatment strategies according to the COPD stage (Table 4). For patients with GOLD I disease, they mainly prescribed short acting β_2-agonists (SABA) and short acting anti-cholinergics (SAAC), both administered by inhalation via pMDIs or DPIs. The strategies changed for the higher GOLD stages (II to IV): fewer SABA and SAAC were prescribed, and when prescribed for advanced COPD, nebulisation was used instead of pMDI or DPI. Also, more long acting anti-cholinergics (LAAC) and long acting β_2-agonists (LABA) were used in combination with inhaled corticosteroids in advanced COPD. In contrast to the GOLD guidelines 2010, oral corticosteroids were prescribed surprisingly often (15 and 34% for GOLD III and GOLD IV). For those patients with higher GOLD stages, the usual prescription was a fixed combination of inhaled corticosteroids and LABA (ICS/LABA, 24% for GOLD II, but 91 and 94% for GOLD III and GOLD IV), or mucolytics. Theophylline, oxygen, and physiotherapy were mainly prescribed for GOLD III and IV.

Patients follow-up

Most PPs did the patient follow-up themselves (64%), while a third of them delegated that responsibility to a GP (35%).

Nearly all PPs declared that they used symptoms to determine the follow-up treatment of their patients (Table 5); most of them also used pulmonary function, external risk factors, exacerbations, clinical examination, patient's mobility or co-morbidities. Quality of life and family history of COPD were reported by a minority of PPs, but objective questionnaires were rarely used (10%) to assess the quality of life. Similarly, the MRC dyspnoea scale was mentioned by only a few PPs (8%). Some of them said they used arterial blood gas analysis (8%) or high resolution computed tomography (2%) for their follow-up treatment decision.

Dyspnoea, expectorations, and frequent or persistent cough were most often cited as specific symptoms to determine follow-up care, although the frequencies ranged from 15% to 19% (Table 5). Smoking was more frequently stated as a specific risk factor than exposure to chemical substances or air pollution and asthma.

Variability of symptoms during the day

The majority of PPs recognised that COPD symptoms vary throughout the day. They agreed to various extents that all

Table 4: COPD treatment strategies according to the GOLD[a] stage of the patient

Strategies		GOLD I (%)	GOLD II (%)	GOLD III (%)	GOLD IV (%)
Short acting β_2-agonists	Inhalation via DPI	90	66	62	59
	Nebulisation	0	1	4	17
Long acting β_2-agonists		4	48	40	36
Short acting anti-cholinergics	Inhalation	59	48	45	41
	Nebulisation	0	0	3	15
Long acting anti-cholinergics		7	79	79	79
Oral corticosteroids		1	5	15	34
Inhaled corticosteroids	Low daily dose[b]	3	12	9	4
	Moderate daily dose	0	9	45	27
	High daily dose	0	0	13	30
Fixed combination (ICS/LABA[c])		0	24	94	91
Leukotriene antagonists		0	0	1	2
Theophylline		1	5	16	51
Mucolytics		9	24	44	53
Oxygen		2	3	22	89
Physiotherapy		3	17	59	76
Others		2	3	8	10

Data analysed according to information recorded in the returned questionnaires (N = 116). The respondents could choose more than one item, therefore the totals do not add to 100%.
COPD: Chronic Obstructive Pulmonary Disease
[a] GOLD: Global Initiative for Chronic Obstructive Lung Disease.
[b] Low dose: ≤ 500 µg BDP/day; moderate dose: > 500-1000 µg BDP/day; high dose: > 1000 µg BDP/day
[c] ICS/LABA: inhaled corticosteroid/long-acting β_2-agonists.

Table 5: Criteria used for determining follow-up care for COPD patients

Parameters	Used by PPs (%)
Symptoms	99
Dyspnoea	19
Expectorations	16
Frequent/persistent cough	15
Tightness	12
Morning symptoms	12
Wheezing	11
Nocturnal awakening	8
Fatigue	6
Others	1
Pulmonary function	91
Exposure to external risk factors	91
Smoking	46
Chemical substances	22
Pollution	22
Asthma	10
Exacerbation	86
Clinical examination	79
Patient's mobility	68
Co-morbidities	56
Quality of life	40
Other	19
Family history of COPD	13
MRC dyspnoea scale	8

Data analysed according to information recorded in the returned questionnaires (N = 116).
COPD: Chronic Obstructive Pulmonary Disease
MRC: Medical Research Council.

respiratory symptoms had the highest intensity in the morning (Figure 1). In particular, most PPs noted cough with expectoration (92%), dyspnoea (89%), and frequent or persistent cough (75%), while wheezing and tightness were reported by half of them (59% and 51%, respectively). General symptoms were observed more often at other times of the day: loss of appetite at noon (33%), fatigue mostly in the afternoon (41%), and depression/anxiety (48%) in the evening.

When asked if the variability of symptoms during the day impacted the quality of life and the mobility of the patients, 97% of the PPs declared that it affected the quality of life, and 89% of the PPs said it affected the mobility of patients. Most PPs believed that impairments in mobility occurred mainly in the morning (84%), and much less at other times of the day (16% stated at noon, 9% the afternoon, 6% in the evening, and 5% at night).

Finally, 69% of the PPs declared that they would change their therapeutic strategy for the COPD patients with more severe morning symptoms. In particular, they suggested to take the medication earlier (49%), to increase the dose of bronchodilatators (21%) and to a lesser extent that of inhaled corticosteroids (7%). Other treatment modifications are listed in Table 6.

DISCUSSION

To our knowledge, data on the awareness and treatment strategies of COPD are not available for Belgium and the present survey fills the gap. 116 experienced PPs representing nearly all geographical areas of Belgium reported that they assessed COPD diagnosis and severity based on a combination

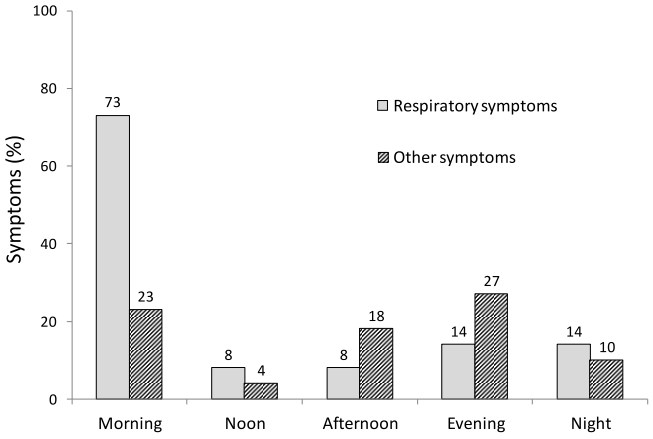

Figure 1: *Intensity of COPD symptoms as evaluated by PPs*
The intensity of symptoms during the day was assessed by the pulmonologists during patients' follow-up visits. Results were pooled as respiratory symptoms (cough with expectoration, dyspnoea, frequent or persistent cough, wheezing, and tightness) or other symptoms (depression/anxiety, loss of appetite, fatigue, and other) and expressed as average percentage in function of the time of the day (morning: 6-10 h; noon: 10-14 h; afternoon: 14-18 h; evening: 18-22 h; night: 22-6 h). Several time periods could be checked for each symptom.

Table 6: Impact on therapeutic strategy of severe morning symptoms

Modified therapeutic strategies	%
Take medication earlier	49
Increase dose	28
Start faster acting treatments	25
Pulmonary rehabilitation	23
Add another medication	20
Replace one of the medications	5
Other	2

Data analysed according to information recorded on pulmonologists' questionnaires (N = 116).
Several therapeutic strategies could be checked.

of parameters and confirmed diagnosis with spirometry. Their main treatment objectives were symptom relief, prevention of exacerbations, and improvement of quality of life. When those objectives could not be reached, most of them would add another medication to the treatment regimen before increasing the dose or make other treatment modifications. As expected, treatment strategies were modulated according to the COPD stage, with short-acting drugs and nebulised administration prescribed for incipient COPD, while long-acting drugs and formulations inhaled via pMDIs or DPIs were prescribed mainly for advanced stages, together with ICS and fixed combination ICS/LABA. The PPs observed that a variability of symptoms during the day, particularly in the morning, affected the quality of life and mobility of their patients. A worsening of respiratory symptoms in the morning influenced their therapeutic strategy towards recommending medication be taken earlier in the day, increasing the dose, adding another medication or pulmonary rehabilitation.

Our study confirms the impact of morning symptoms on the quality of life in COPD patients, which was already described by Kessler et al (23) and Partridge et al (24-25). We also showed that respiratory symptoms are more frequent in the morning, while other symptoms are more prevalent in the afternoon and the evening (Figure 1). The most cited strategy to treat severe morning symptoms was to advise to take medication earlier. This could have implications towards the general management of COPD patients: intake of bronchodilatators could be advised before leaving bed, especially bronchodilatators with fast onset.

The present survey was conducted in line with new developments in the knowledge, detection and treatment of COPD for a better understanding of early stages of the disease (16). Our study extends the survey conducted by Vandevoorde et al. (11) which was restricted to the detection of COPD in a population of at-risk patients (current smokers with a smoking history of at least 15 pack-years). In this survey, 37% of the COPD patients were diagnosed during their first visit to a PP. This underscores the need for improved COPD detection in primary care. In particular, GPs should systematically refer smokers or ex-smokers with suggestive complaints to a PP to perform a spirometry test to objectively detect COPD, or perform the spirometry test themselves (after appropriate training). Patients often do not seek medical help until they have more advanced symptoms. Furthermore, the poor correlation between symptoms and the degree of lung function impairment in the early stages of COPD is well documented. This situation will probably evolve towards a better usage of diagnostic parameters, as the revision of the GOLD guideline recommends a quantitative method to assess symptoms severity (mMRC dyspnoea score or COPD Assessment Test [CAT] score) (3). Our data were collected before the 2011 GOLD update was issued, hence under reporting the use of symptoms scores (MRC dyspnea score, CAT score) as marker of COPD severity.

The international BOLD study reported a higher than expected prevalence (10% of the general population) of stage II or higher COPD (6). Based on the last 10 new COPD patients of these PPs, our data also revealed a high prevalence of GOLD stages II to IV (86%) among Belgian COPD patients. It should be stressed that this repartition over the GOLD severity stages pertains to pulmonary physicians and not to general practitioners. It is expected that the latter would reflect better the severity seen in the general population.

We have shown that, although these PPs used spirometry, symptoms, and exposure to risk factors to confirm COPD, the key indicators recommended by the GOLD guidelines 2010 were not used routinely, namely dyspnoea (19%), chronic cough (18%), and chronic sputum production (16%). However, the questionnaire used in this survey did not further investigate the reasons for these low frequencies. It was also surprising that only 41% of the PPs used smoking history as a diagnostic criterion, knowing that 90% of the COPD patients in our countries are smokers or ex-smokers. This unexpected low usage could result from the design of the questionnaire.

In general, the self-declared management of COPD by Belgian PPs is reasonably well in line with the GOLD guidelines 2010. Nevertheless, at least three elements in the present survey deviate from these guidelines.

First, 84% of Belgian PPs use the percentage of FEV_1 predicted in the diagnosis of COPD (2% for diagnosis only and 82% for diagnosis and assessment of severity), whereas strictly according to the guidelines it should only be used for the assessment of severity. Conversely, the FEV_1/FVC ratio was used for the assessment of severity by 3% of PPs and by 64% of PPs for diagnosis and assessment of severity, while it should only be used for diagnosis. This is because in the latter stages of the disease, disease progression will reduce both FEV_1 and FVC. Hence, severity will increase while the FEV_1/FVC ratio remains unchanged. It should also be noted that a recent Belgian study showed that in current practice, patients referred to a PP by their GP for differential diagnosis are usually submitted to a heterogeneous series of tests (26).

Second, the use of a bronchodilator test is needed in spirometry to assess the reversibility of the airflow obstruction. Our survey did not differentiate between spirometry performed with or without a bronchodilator, which can potentially lead to an overestimation of COPD prevalence (27). Only 74% of PPs used the percent reversibility of FEV_1 as a relevant parameter, and 11% of the PPs considered this parameter a measure for the severity of COPD rather than a diagnostic argument.

Third, oral steroids are still commonly prescribed in GOLD stage III and IV patients, while strictly there are no indications for chronic treatment with these drugs in COPD. Indeed the side-effects of oral steroids often outweigh the benefits (28). However, the excess use of oral steroids in these patients might be the sign of an overall worsening in the COPD population over the years and needs further study.

It should be noted that the use of LABA reported by the PPs in this survey was collected before indacaterol (a once-daily LABA) was available on the Belgian market.

The results of this survey should be read in the light of several methodological limitations. We did not ask if another spirometry test was performed 6 to 8 weeks later. This would confirm that the patient had indeed COPD and avoid possible confusion with asthma (27).

The recruitment of PPs via medical representatives could also have introduced a bias as we cannot confirm that all Belgian PPs were visited on time for the survey; factors such as unavailability, absence, or visit denial make it unlikely that all PPs received the questionnaire on time. Nevertheless, responders were distributed in all geographical areas of Belgium, Walloon Brabant being probably assimilated with Brussels' area.

The response rate of 25% also limits the generalisation of our results, although it is not surprising given that participation to the survey was not compulsory and no incentive of any kind was ever linked to the invitation to the AstraZeneca meetings. The response rate in our study is similar to that obtained in a previous survey (29) performed among all Belgian PPs in December 2001 – January 2002, with a response rate of 24%. At that time, the repartition of responders was distributed between 59% in Dutch speaking areas and 41% in French speaking areas, which is comparable to our study, with 49% in Dutch and 37% in French speaking areas, respectively (to the exclusion of 10% of responders in Brussels and 4% unspecified). We can therefore assume that in spite of a modest response rate, our results are representative of the Belgian PPs habitual practice.

It was striking that PPs were well aware of the importance of morning symptoms, particularly dyspnoea, cough with expectoration, and frequent or persistent cough. These symptoms were also recognised to affect quality of life and mobility. The observation is striking, as the literature on these symptoms in COPD is relatively scarce and recent (23-25). This suggests that the occurrence of morning symptoms and their consequences for quality of life and mobility is likely to be a common clinical observation and further confirms the importance of these symptoms.

In conclusion, this survey showed that Belgian PPs had an acceptable self-declared adherence to the GOLD guidelines 2010, although some clear discrepancies were present as well. These discrepancies pertained to the use of symptoms and pulmonary function variables in the diagnosis of COPD and the overuse of chronic treatment with oral corticosteroids. In contrast to our expectations, Belgian PPs were well aware of morning symptoms and their impact on patients' lives.

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All authors contributed to the design of the survey and to the writing of the manuscript. The decision to submit was borne by all authors.

CONFLICT OF INTEREST

The authors declare the following conflicts of interest: Guy G. Brusselle has, within the last 5 years, received honoraria for lectures from AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline, MerckSharp&Dohme, Novartis, Pfizer and UCB; he is a member of advisory boards for AstraZeneca, Boehringer-Ingelheim, GlaxoSmithKline and Novartis. Johan Buffels has received unconditional research grants from AstraZeneca and Boehringer Ingelheim, and consultancy honoraria from AstraZeneca, GlaxoSmithKline, UCB and Zambon. Louis Corhay has received consultancy honoraria from AstraZeneca, Boehringer Ingelheim/Pfizer, GlaxoSmithKline, Novartis and Nycomed. Wilfried De Backer received for his institution unrestricted grants from AstraZeneca, GSK and Chiesi. Marc Decramer is part of advisory boards of AstraZeneca, GSK, Boehringer/Pfizer, Novartis, Nycomed and Dompé; he gave lectures for these companies and he received research grants from AstraZeneca, GSK and Boehringer. Jean-Marie Degryse has received unconditional research grants from Boehringer Ingelheim, AstraZeneca and GlaxoSmithKline Biologicals. Wim Janssens has received consultancy and lecturing honoraria from AstraZeneca, Boehringer, Ingelheim/Pfizer, GlaxoSmithKline and Novartis. Eric Marchand has received has received consultancy honoraria from AstraZeneca, Boehringer Ingelheim/Pfizer, and GlaxoSmithKline.

Véronique Van Craenendonck and Hans Vandenberghe are employees of AstraZeneca. Paul Van den Brande has received consultancy honoraria from AstraZeneca and Chiesi. Walter Vincken has received consultancy honoraria from AstraZeneca, Boehringer Ingelheim/Pfizer, GlaxoSmithKline, Meda, Novartis, Nycomed and UCB.

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REFERENCES

1. Raherison C, Girodet P-O. Epidemiology of COPD. *Eur Respir Rev* 2009; 18: 213-221.
2. Radin A, Cote C. Primary care of the patient with Chronic Obstructive Pulmonary Disease – Part 1: Frontline prevention and early diagnosis. *Am J Med* 2008; 121(S1): S3–S12. doi: 10.1016/j.amjmed.2008.04.002.
3. Global Strategy for Diagnosis, Management, and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011. Available from http://www.goldcopd.org. Last accessed on August 20, 2012.
4. Decramer M, Miravitlles M, Price D, et al. New horizons in early stage COPD – Improving knowledge, detection and treatment. *Respir Med* 2011; 105: 1576-1587. doi: 10.1016/j.rmed.2010.12.015.
5. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *ERJ* 2006; 28: 523-532.
6. Buist S, McBurnie MA, Vollmer W, et al. International variation in the prevalence of COPD (The BOLD Study): a population-based prevalence study. *Lancet* 2007; 370: 741-750.
7. Perez X, Wisnivesky JP, Lurslurchachai L, Kleinman LC, Kronish IM. Barriers to adherence to COPD guidelines among primary care providers. *Respir Med* 2012; 106: 374-381. doi: 10.1016/j.rmed.2011.09.010. Epub 2011 Oct 13.
8. Schirnhofer L, Lamprecht B, Vollmer WM, et al. COPD prevalence in Salzburg, Austria: results from the Burden of Obstructive Lung Disease (BOLD) Study. *Chest* 2007; 131: 29-36.
9. Monteagudo M, Rodriguez-Blanco T, Parcet J, et al. Variability in the performing of spirometry and its consequences in the treatment of COPD in primary care. *Archivos de Bronconeumología* 2011; 47: 226-233.
10. Joo MJ, Lee TA, Weiss KB. Geographic variation of spirometry use in newly diagnosed COPD. *Chest* 2008; 134: 38-45.
11. Vandevoorde J, Verbanck S, Gijssels L, et al. Early detection of COPD: a case finding study in general practice. *Respir Med* 2007; 101: 525-530.
12. Buffels J, Degryse J, Heyrman J, Decramer M; DIDASCO Study. Office spirometry significantly improves early detection of COPD in general practice: the DIDASCO study. *Chest* 2004, 125: 1394-1399.
13. Jenkins CR, Jones PW, Calverley PM, et al. Efficacy of salmeterol/fluticasone propionate by GOLD stage of chronic obstructive pulmonary disease: analysis from the randomised, placebo-controlled TORCH study. *Respir Res* 2009, 10: 59.
14. Decramer M, Celli B, Kesten S, Lystig T, Mehra S, Tashkin DP; UPLIFT investigators. Effect of tiotropium on outcomes in patients with moderate chronic obstructive pulmonary disease (UPLIFT): a prespecified subgroup analysis of a randomized controlled trial. *Lancet* 2009, 374: 1171-1178.
15. Decramer M, Cooper CB. Treatment of COPD: the sooner the better? *Thorax* 2010; 65: 837-841.
16. Decramer M, Miravitlles M, Price D, et al. New horizons in early stage COPD – Improving knowledge, detection and treatment. *Respir Med* 2011, 105: 1576-1587. doi: 10.1016/j.rmed.2010.12.015.
17. Welte T. Optimizing treatment for COPD – new strategies for combination therapy. *IJCP* 2009; 63: 1136-1149.
18. Vincken W. An update on bronchodilator treatment of chronic obstructive pulmonary disease (COPD). *Ann Respir Med* 2012; 1(2): 1-16.
19. Rabe K. Improving dyspnea in chronic obstructive pulmonary disease. Optimal treatment strategies. *Proc Am Thorac Soc* 2006; 3: 270-275.
20. Brand PL, Postma DS, Kerstjens HA, Koëter GH. Relationship of airway hyperresponsiveness to respiratory symptoms and diurnal peak flow variation in patients with obstructive lung disease. The Dutch CNSLD Study Group. *Am J Respir Crit Care Med* 1991; 143: 916-921.
21. Kerstjens HA, Brand PL, de Jong PM, Koëter GH, Postma DS. Influence of treatment on peak expiratory flow and its relation to airway hyperresponsiveness and symptoms. The Dutch CNSLD Study Group. *Thorax* 1994; 49: 1109-1115.
22. McCarley C. A pilot home study of temporal variations of symptoms in chronic obstructive lung disease. *Biol Res Nurs* 2007; 9: 8-20.
23. Kessler R, Partridge MR, Miravitlles M, et al. Symptom variability in patients with severe COPD: a pan-European cross-sectional study. *ERJ* 2011; 37: 264-272.
24. Partridge MR, Karlsson N, Small IR. Patient insight into the impact of chronic obstructive pulmonary disease in the morning: an internet survey. *Curr Med Res Opin* 2009; 25: 2043-2048.
25. Partridge MR, Cazzola M, Kessler R, et al. Diurnal variation of symptoms and impact on morning activities in severe COPD: a pan-European cross-sectional study. *Eur Respir Soc*, ERS Annual Congress, Vienna 2009, Abstract 970.
26. Buffels J, Degryse J, Liistro G, Decramer M. Differential diagnosis is a primary care population with presumed airway obstruction: A real-life study. *Respiration* 2012; 84: 44-54. Epub 2001 Nov 15. doi: 10.1159/000332836.
27. Price DB, Yawn BP, Jones RCM. Improving the Differential Diagnosis of Chronic Obstructive Pulmonary Disease in Primary Care. *Mayo Clin Proc* 2010; 85: 1122-1129.
28. Dekhuijzen PN, Decramer M. Steroid-induced myopathy and its significance to respiratory disease: a known disease rediscovered. *Eur Respir J* 1992; 5: 997-1003.
29. Decramer M, Bartsch P, Pauwels R, Yernault JC and the COPD Advisory Board. Management of COPD according to guidelines. A national survey among Belgian physicians. *Monaldi Arch Chest Dis* 2003; 59: 62-80.

Appendix:

COPD Awareness Program SP questionnaire

Treatment schedule COPD

Dear Doctor,

Thank you for filling in this questionnaire.

This survey will allow us to understand the treatment schedules you are using for your COPD patients in your daily practice. We will also try to determine whether the symptoms your COPD patients experience, are variable over the course of the day.

May we ask you to fill in this questionnaire as precisely as possible?

We would also like to clarify that all collected data in the framework of this study will be handled in a completely anonymous manner. Your data will be merged with data from your colleagues in order to attain a global analysis at the Belgian level.

Sincerely yours,

Prof. Dr. M. Decramer
President, COPD Working Group

Years of Practice Experience:

_____ **Years**

Province:

_____

1. Patients

1.1 How many COPD (chronic obstructive pulmonary disease) patients do you see on average in a representative month in your practice?

☐ Patients per month

Patient's referral source

1.2 When you think of the last 10 new COPD patients who came for a consultation, how many were:

☐ patients who had not yet been diagnosed and/or treated ……/10
☐ COPD patients who had already been diagnosed and/or treated ……/10

TOTAL = 10 patients

1.3 Can you specify where these last 10 new COPD patients were referred from?

☐ Patient was referred by the general practitioner ……/10
☐ Patient came on own initiative ……/10
☐ Patient was referred by a colleague of a different specialty ……/10
Which specialty? ……

TOTAL = 10 patients

Diagnosis and severity evaluation

1.4 In how many of these last 10 new COPD patients was the diagnosis, based on spirometry, determined by:

☐ yourself ……/10
☐ the general practitioner ……/10
☐ a colleague of a different specialty ……/10
Which specialty? ……

TOTAL = 10 patients

1.5 How would you classify these last 10 new COPD patients?

☐ GOLD stage I ……/10
☐ GOLD stage II ……/10
☐ GOLD stage III ……/10
☐ GOLD stage IV ……/10

TOTAL = 10 patients

1.6 Which parameters do you take into account when determining the diagnosis and/or the COPD severity stage?

Please specify whether this applies to the diagnosis and/or severity of the disease.

☐ **Symptomatology** (☐ Diagnosis / ☐ Severity / ☐ Both)
o Wheezing o Tightness o Frequent/chronic coughing

o Expectorations o Waking up at night o Dyspnoea
o Morning symptoms o Fatigue o Other: ……

☐ **Family history of COPD** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **Exposure to risk factors** (☐ Diagnosis / ☐ Severity / ☐ Both)
o Smoking o Pollution o Chemical substances o Asthma

☐ **Patient's quality of life** (☐ Diagnosis / ☐ Severity / ☐ Both)
o Measured by means of an objectively validated questionnaire (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **Patient's mobility (ability to perform daily tasks)**
(☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **Occurrence of exacerbations** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **Co-morbidities** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **Questionnaires (e.g. MRC questionnaire)** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **Patient's physical examination** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **Pulmonary function** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **Other:** …… (☐ Diagnosis / ☐ Severity / ☐ Both)

1.7 When you perform spirometry, which parameter do you use to determine the diagnosis and COPD severity?

☐ **FEV1 (% of the predicted value)** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **FVC (% of the predicted value)** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **FEV1/FVC** (☐ Diagnosis / ☐ Severity / ☐ Both)

☐ **% reversibility of FEV1** (☐ Diagnosis / ☐ Severity / ☐ Both)

Therapeutic goals

1.8 When you initiate treatment for a COPD patient, which are the 3 most important goals to you (in order of importance, with 1 = most important)?

☐ …… Symptom relief
☐ …… Improvement of morning symptoms
☐ …… Prevention of worsening of pulmonary function
☐ …… Prevention of exacerbations
☐ …… Prevention of hospitalisations
☐ …… Prevention of oral corticosteroids use
☐ …… Prevention of antibiotics use
☐ …… Decrease in mortality

- ☐ …… Prevention or minimisation of adverse effects of the treatment
- ☐ …… Prevention and treatment of COPD complications
- ☐ …… Improvement of patients' quality of life
- ☐ …… Improvement of patients' mobility (ability to perform daily tasks)
- ☐ …… Other, please specify

1.9 What do you do if the initiated treatment does not reach therapeutic goals?

- ☐ Increase the dose of one of the medicines
- ☐ Add a medicine to the current therapy
- ☐ Switch the medicine
- ☐ Other type of treatment change: ……

Treatment strategy

1.10 When you think of your last 10 new COPD patients, in how many patients was treatment initiated by:

- ☐ yourself ……/10
- ☐ the general practitioner ……/10
- ☐ a colleague of another specialty ……/10

  Which specialty?

TOTAL = 10 patients

1.11 We will now ask you to specify the treatment you usually prescribe for COPD GOLD stage I, II, III and IV patients. Please specify the initial treatment for each group by using the table below. *(Indicate with an 'x')*

	Gold stage I	Gold stage II	Gold stage III	Gold stage IV
Short-acting β2-mimetics	☐ via inhalation ☐ via nebulisation	☐ via inhalation ☐ via nebulisation	☐ via inhalation ☐ via nebulisation	☐ via inhalation ☐ via nebulisation
Long-acting β2-mimetics				
Short-acting Anticholinergics	☐ via inhalation ☐ via nebulisation	☐ via inhalation ☐ via nebulisation	☐ via inhalation ☐ via nebulisation	☐ via inhalation ☐ via nebulisation
Long-acting Anticholinergics				
Oral corticosteroids				
Inhalation corticosteroids low daily dose: < 500 µg BDP/day moderate daily dose: > 500 µg BDP/day high daily dose: < 500 µg BDP/day	 ☐ low daily dose ☐ moderate daily dose ☐ high daily dose	 ☐ low daily dose ☐ moderate daily dose ☐ high daily dose	 ☐ low daily dose ☐ moderate daily dose ☐ high daily dose	 ☐ low daily dose ☐ moderate daily dose ☐ high daily dose
Fixid combinations (ICS/LABA)				
Leukotriene receptor-antagonists				
Theophylline				
Mucolytics				
Oxygen				
Physical therapy				
Other (specify)				

Patient follow-up

1.12 When you think of your last 10 new COPD patients, how many patients had treatment follow-up done by:

☐ yourself ……/10

☐ the general practitioner ……/10

☐ a colleague of another specialty ……/10

Which specialty?

TOTAL = 10 patients

1.13 Which parameters do you take into consideration when you do COPD patient follow-up?

☐ **Symptomatology**

o Wheezing o Tightness o Frequent/chronic coughing
o Expectorations o Waking up at night o Dyspnoea
o Morning symptoms o Fatigue o Other: ……

☐ **Family history of COPD**

☐ **Exposure to risk factors**

o Smoking o Pollution o Chemical substances o Asthma

☐ **Patient's quality of life**

o Measured by means of an objectively validated questionnaire

☐ **Patient's mobility (ability to perform daily tasks)**

☐ **Occurrence of exacerbations**

☐ **Co-morbidities**

☐ **Questionnaires (e.g. MRC questionnaire)**

☐ **Patient's physical examination**

☐ **Pulmonary function**

☐ **Other:** ……

1. Symptom variability

2.1 Do you think that symptoms related to COPD can be variable over the course of the day?

☐ Yes

☐ No

2.2 If yes, can you indicate with an 'x' for each symptom when you think they are most severe (at what time of the day)?

You can indicate multiple time periods

	Morning (between 6am and 10 am)	Noon (between 10am and 2 pm)	Afternoon (beween 2pm and 6pm)	Evening (between 6pm and 10pm)	Night (between 10pm and 6am)
Dyspnea					
Wheezing					
Frequent or continuous coughing					
Cough with expectorations					
Fatigue					
Tightness					
Lack of appetite					
Depression/Fear					
Other:					

2.3 Do you think that the variability of these symptoms over the course of the day has an impact on your COPD patients' quality of life?

☐ Yes

☐ No

2.4 Do you think that the variability of these symptoms over the course of the day has an impact on your COPD patients' mobility?
Mobility is hereby defined as the ability to perform daily tasks.

☐ Yes

☐ No

2.5 If yes, please indicate with an 'x' when, according to you, the variability of symptoms has the most impact on your COPD patients' mobility?

Morning (between 6am and 10 am)	Noon (between 10am and 2 pm)	Afternoon (beween 2pm and 6pm)	Evening (between 6pm and 10pm)	Night (between 10pm and 6am)

2.6 If you indicated that the symptoms your patients experience are the most severe over the course of the morning (between 6am and 10am), does this have an impact on your therapeutic approach?

☐ Yes

☐ No

2.7 If yes, which?

☐ You increase the dose:
o inhalation corticosteroids o bronchodilators

☐ You recommend that the patient take his/her medication earlier in the morning

☐ You add a medicine to the current treatment

☐ You start treatment with a quicker effect

☐ You replace one of the medicines

☐ You initiate treatment with pulmonary revalidation

☐ Other: ……

Thank you for your collaboration!